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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,643	03/06/2006	George Coukos	555-88	7985

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EXAMINER	
DIBRINO, MARIANNE NMN	
ART UNIT	PAPER NUMBER
1644	
MAIL DATE	DELIVERY MODE
12/24/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/525,643	COUKOS ET AL.	
	Examiner	Art Unit	
	MARIANNE DIBRINO	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9 and 11-30* is/are pending in the application.

4a) Of the above claim(s) *1-8,11 and 19-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9 and 12-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed 8/18/09 is acknowledged and has been entered.

2. Applicant is reminded of Applicant's election with traverse of Group II (claims 9-18) and species of nucleic acid sequence encoding the sequence of SEQ ID NO: 8 in Applicant's response filed 12/23/08.

Claims 9 and 12-18 are currently being examined.

3. Applicant is reminded that the disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, for example at the paragraph beginning on page 25 at line 6. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP§ 608.01.

Although Applicant has submitted a replacement paragraph in the amendment filed 8/18/09, the said paragraph still contains embedded hyperlinks (*i.e.,* http://www...) and in addition, it also contains other browser-executable code (*i.e.,* http://..., for example, http://pbil.ibcp.fr/).

4. Applicant's amendment filed 8/18/09 has overcome the prior rejection of record of claims 9, 10 and 12-18 under 112, first paragraph, as failing to comply with the written description requirement.

5. Applicant's amendment filed 8/18/09 has overcome the prior rejection of record of claims 9, 10 and 12-18 under 35 U.S.C. 112, first paragraph, scope of enablement.

6. For the purpose of prior art rejections, the filing date of the instant claims 9 and 12-18 is deemed to be the filing date of PCT/US03/27488*, i.e.,* 9/4/03, as the provisional parent applications 60/408,397 and 60/478,371 do not support the claimed limitations of the instant application. At a minimum, 60/408,397 does not have support for an isolated nucleic acid molecule *comprising* SEQ ID NO: 21 or a nucleic acid molecule complemetary thereto, nor the vector comprising the said nucleic acid molecule, including wherein the vector is a viral vector, nor wherein the nucleic acid molecule is operably linked to a promoter, including a tumor specific promoter, nor a host cell comprising the said vector, including a mammalian cell, nor the claimed method of culturing the host cell to produce the encoded polypeptide. At a minimum, 60/478,371 does not have support for a nucleic acid molecule comprising SEQ ID NO: 21 or its complement, nor the said recited genus and species of vector or host cells or method of culturing the host cell to produce the encoded polypeptide.

7. Applicant's amendment filed 8/18/09 has overcome the prior rejections of record of claims 9, 10, 12-14 and 16-18 under 35 U.S.C. 102(a) and 102(3) as being anticipated by WO 03/029436 A2 (4/10/03, of record).

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 9, 12-14 and16 stand rejected under 35 U.S.C. 102(a) as being anticipated by Chalupny *et al* (Biochem. Biophys. Res. Comm. 305: 129-135, 5/23/03, IDS reference).

Chalupny *et al* teach an isolated cDNA encoding ULBP4, a viral vector comprising said cDNA operably linked to a promoter and a host cell comprising said vector (especially materials and methods, Figure 1, page 132 at the second full paragraph at column 2).

Although Chalupny *et al* do not explicitly teach the nucleotide bases 1-60 (presumably a signal sequence) of SEQ ID NO: 21 recited in instant claim 9, Chalupny *et al* do teach a bacterial artificial chromosome comprising the nucleic acid molecule from which the open-reading frame of Letal (ULBP4) was deduced. Therefore the claimed nucleic acid molecule appears to be the same as the nucleic acid molecule of the prior art absent a showing of differences. Since the Patent Office does not have the facilities for examining and comparing the composition of the instant invention to those of the prior art, the burden is on Applicant to show a distinction between the nucleic acid molecule of the instant invention and that of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Applicant's arguments in the amendment filed 8/18/09 have been fully considered but are not persuasive, given the inherent teaching of the signal sequence of ULBP4.

Applicant argues that the claims have been revised to make reference to the sequence of SEQ ID NO: 21. However, nucleotide bases 1-60 of SEQ ID NO: 21 recited in instant claim 9 presumably encode a signal sequence, SEQ ID NO: 21 encodes Letal or ULBP4, and the art reference teaches a nucleic acid molecule that encodes ULBP4, including the signal sequence.

10. Claims 9, 12-14 and 16 stand rejected under 35 U.S.C. 102(a) as being anticipated by Conejo-Garcia *et al* (Cancer Biol. & Ther. 2(4): e112-e117, July/August, 2003, IDS reference).

Conejo-Garcia *et al* teach isolated cDNA encoding Letal (ULBP4), a retroviral vector comprising the said cDNA operably linked to a promoter, and a host cell comprising said

vector (see entire reference, especially Results section at column 2 on page e114 and continuing onto the paragraph at column 1 on page e115).

Although Conejo-Garcia *et al* do not explicitly teach the nucleotide bases 1-60 (presumably a signal sequence) of SEQ ID NO: 21 recited in instant claim 9, Conejo-Garcia *et al* do teach the nucleic acid molecule from which the open-reading frame of Letal was deduced. Therefore the claimed nucleic acid molecule appears to be the same as the nucleic acid molecule of the prior art absent a showing of differences. Since the Patent Office does not have the facilities for examining and comparing the composition of the instant invention to those of the prior art, the burden is on Applicant to show a distinction between the nucleic acid molecule of the instant invention and that of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Applicant's arguments in the amendment filed 8/18/09 have been fully considered but are not persuasive, given the inherent teaching of the signal sequence of ULBP4.

Applicant argues that the claims have been revised to make reference to the sequence of SEQ ID NO: 21. However, nucleotide bases 1-60 of SEQ ID NO: 21 recited in instant claim 9 presumably encode a signal sequence, SEQ ID NO: 21 encodes Letal or ULBP4, and the art reference teaches a nucleic acid molecule that encodes ULBP4, including the signal sequence.

11. Applicant's amendment filed 8/1/09 has overcome the prior rejection of record of claims 9, 10 and 12-18 under 35 U.S.C. 103(a) as being unpatentable over WO 03/029436 A2 (4/10/03) in view of Katabi *et al* (Human Gene Therapy 10: 155-164, 1999, of record).

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 9 and 12-16 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Conejo-Garcia *et al* (Cancer Biol. & Ther. 2(4): e112-e117, July/August, 2003, IDS reference) in view of Katabi *et al* (Human Gene Therapy 10: 155-164, 1999, of record).

During patent examination, the pending claims must be "given the broadest reasonable interpretation consistent with the specification." Applicant always has the opportunity to amend the claims during prosecution and broad interpretation by the Examiner reduces the possibility that the claim, once issued, will be interpreted more broadly than is justified. In re Prater, 162 USPQ 541, 550 - 51 (CCPA 1969).

It is noted by the Examiner that the limitation "tumor specific promoter" is not defined in the instant specification. The specification at [0033] discloses only some examples of tumor specific promoters.

Conejo-Garcia *et al* teach isolated cDNA encoding Letal (ULBP4), a retroviral vector comprising the said cDNA operably linked to a promoter, and a host cell comprising said vector (see entire reference, especially Results section at column 2 on page e114 and continuing onto the paragraph at column 1 on page e115). Conejo-Garcia *et al* further teach that expansion of specific T-cells at tumor sites can be boosted by engineering cells with higher levels of Letal or using soluble forms of the ligand.

Conejo-Garcia *et al* do not teach wherein the promoter is a tumor specific promoter. Katabi *et al* teach use of tumor-selective, *i.e.,* specific, promoters in targeted gene therapy for cancer (especially abstract and overview summary sections).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used a tumor-specific promoter as taught by Katabi *et al* in the vector construct taught by Conejo-Garcia *et al*.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to expand specific T-cells at tumor sites by engineering cells with higher levels of Letal as taught by Conejo-Garcia *et al*.

Although Conejo-Garcia *et al* do not explicitly teach the nucleotide bases 1-60 (presumably a signal sequence) of SEQ ID NO: 21 recited in instant claim 9, Conejo-Garcia *et al* do teach the nucleic acid molecule from which the open-reading frame of Letal was deduced. Therefore the claimed nucleic acid molecule appears to be similar to the nucleic acid molecule of the prior art absent a showing of unobvious differences. Since the Patent Office does not have the facilities for examining and comparing the composition of the instant invention to those of the prior art, the burden is on Applicant to show an unobvious distinction between the nucleic acid molecule of the instant invention and that of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Applicant's arguments in the amendment filed 8/18/09 have been fully considered but are not persuasive, given the implicit teaching of the signal sequence of ULBP4.

Applicant argues that the claims have been revised to make reference to the sequence of SEQ ID NO: 21. However, nucleotide bases 1-60 of SEQ ID NO: 21 recited in instant claim 9 presumably encode a signal sequence, SEQ ID NO: 21 encodes Letal or ULBP4, and the art reference teaches a nucleic acid molecule that encodes ULBP4, including the signal sequence.

14. Claims 9, 12-14 and 16-18 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Conejo-Garcia *et al* (Cancer Biol. & Ther. 2(4): e112-e117, July/August, 2003, IDS reference) in view of Searle (Curr. Opin. Biotech. 6:548-552, 1995, of record).

Conejo-Garcia *et al* teach isolated cDNA encoding Letal (ULBP4), a retroviral vector comprising the said cDNA operably linked to a promoter, and a host cell comprising said vector (see entire reference, especially Results section at column 2 on page e114 and continuing onto the paragraph at column 1 on page e115). Conejo-Garcia *et al* teach sequence alignment of Letal with ULBP1, 2 and 3, as well as identification of the signal peptide, the α1 and α2 domains ant the transmembrane and cytoplasmic regions (especially Figure 1 and Results). Conejo-Garcia *et al* further teach that expansion of specific T-cells at tumor sites can be boosted by engineering cells with higher levels of Letal or using soluble forms of the ligand. Conejo-Garcia *et al* teach that Letal has a transmembrane and cytoplasmic domain (Figure 1).

Conejo-Garcia *et al* do not teach a method of producing a polypeptide comprising culturing the mammalian host cell of claim 16 under conditions such that said nucleic acid is expressed and said polypeptide is thereby produced.
Searle teaches a method for producing soluble forms of membrane proteins in mammalian cell lines (see entire reference).
It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have produced soluble forms of the Letal protein taught by Conejo-Garcia *et al* using the expression system taught by Searle.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to produce soluble Letal protein because Conejo-Garcia *et al* teach what nucleic acid sequences encode the extracellular portion *vs* the transmembrane and cytoplasmic portions of Letal, and they further teach boosting expansion of specific T-cells at tumor sites using soluble forms of Letal.

Although Conejo-Garcia *et al* do not explicitly teach the nucleotide bases 1-60 (presumably a signal sequence) of SEQ ID NO: 21 recited in instant claim 9, Conejo-Garcia *et al* do teach the nucleic acid molecule from which the open-reading frame of Letal was deduced. Therefore the claimed nucleic acid molecule appears to be similar to the nucleic acid molecule of the prior art absent a showing of unobvious differences. Since the Patent Office does not have the facilities for examining and comparing the composition of the instant invention to those of the prior art, the burden is on Applicant to show an unobvious distinction between the nucleic acid molecule of the instant invention and that of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

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15. Claims 9 and 12-18 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Chalupny *et al* (Biocehm. Biophys. Res. Comm. 305: 129-135, 5/23/03, IDS reference) in view of Katabi *et al* (Human Gene Therapy 10: 155-164, 1999) and Conejo-Garcia *et al* (Cancer Biol. & Ther. 2(4): e112-e117, July/August, 2003, IDS reference) and Searle (Curr. Opin. Biotech. 6:548-552, 1995, of record).

Chalupny *et al* teach an isolated cDNA encoding ULBP4 (*i.e.,* Letal), a viral vector comprising said cDNA operably linked to a promoter and a host cell comprising said vector (especially materials and methods, Figure 1, page 132 at the second full paragraph at column 2).

Chalupny *et al* do not teach wherein the promoter is a tumor specific promoter.

Katabi *et al* teach use of tumor-selective, *i.e.,* specific, promoters in targeted gene therapy for cancer (especially abstract and overview summary sections).

Conejo-Garcia *et al* teach isolated cDNA encoding Letal (ULBP4), a retroviral vector comprising the said cDNA operably linked to a promoter, and a host cell comprising said vector (see entire reference, especially Results section at column 2 on page e114 and continuing onto the paragraph at column 1 on page e115). Conejo-Garcia *et al* further teach that expansion of specific T-cells at tumor sites can be boosted by engineering cells with higher levels of Letal or using soluble forms of the ligand.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used a tumor-specific promoter/vector construct as taught by Katabi *et al* in place of the one taught by Chalupny *et al*.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order target ULBP4 to a tumor cell to boost levels of Letal as taught by Conejo-Garcia *et al*.

Searle teaches a method for producing soluble forms of membrane proteins in mammalian cell lines (see entire reference).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have produced soluble forms of the Letal protein taught by Chalupny *et al* using the expression system taught by Searle.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to produce soluble Letal protein because Conejo-Garcia *et al* teach what nucleic acid sequences encode the extracellular portion *vs* the transmembrane and cytoplasmic portions of Letal, and they further teach boosting expansion of specific T-cells at tumor sites using soluble forms of Letal.

Although Conejo-Garcia *et al* do not explicitly teach the nucleotide bases 1-60 (presumably a signal sequence) of SEQ ID NO: 21 recited in instant claim 9, Conejo-Garcia *et al* do teach the nucleic acid molecule from which the open-reading frame of Letal was deduced. Therefore the claimed nucleic acid molecule appears to be similar to the nucleic acid molecule of the prior art absent a showing of unobvious differences. Since the Patent Office does not have the facilities for examining and comparing the composition of the instant invention to those of the prior art, the burden is on Applicant to show an unobvious distinction between the nucleic acid molecule of the instant invention and that of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Applicant's arguments in the amendment filed 8/18/09 have been fully considered but are not persuasive, given the implicit teaching of the signal sequence of ULBP4.

Applicant argues that the claims have been revised to make reference to the sequence of SEQ ID NO: 21. However, nucleotide bases 1-60 of SEQ ID NO: 21 recited in instant claim 9 presumably encode a signal sequence, SEQ ID NO: 21 encodes Letal or ULBP4, and the art reference teaches a nucleic acid molecule that encodes ULBP4, including the signal sequence.

16. Claims 9 and 12-18 are objected to because of the following informality: currently amended claim 9 recites "or a nucleic acid complementary thereto" rather than "or a nucleic acid molecule complementary thereto." Appropriate correction is required.

17. No claim is allowed.

18. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

19. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Tuesday, Thursday and Friday.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ram Shukla, can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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